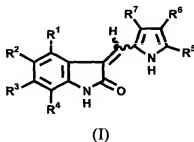


CLAIMS

What is claimed is:

1. A solid formulation, said formulation comprising 5 – 60 % w/w of an indolinone of formula I:



wherein:

R¹ is selected from the group consisting of hydrogen, halo, alkyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, -(CO)R¹⁵, -NR¹³R¹⁴, -(CH₂)_nR¹⁶ and -C(O)NR⁸R⁹;

R² is selected from the group consisting of hydrogen, halo, alkyl, trihalomethyl, hydroxy, alkoxy, cyano, -NR¹³R¹⁴, -NR¹³C(O)R¹⁴, -C(O)R¹⁵, aryl, heteroaryl, and -S(O)₂NR¹³R¹⁴;

R³ is selected from the group consisting of hydrogen, halogen, alkyl, trihalomethyl, hydroxy, alkoxy, -(CO)R¹⁵, -NR¹³R¹⁴, aryl, heteroaryl, -NR¹³S(O)₂R¹⁴, -S(O)₂NR¹³R¹⁴, -NR¹³C(O)R¹⁴, -NR¹³C(O)OR¹⁴ and -SO₂R²⁰ (wherein R²⁰ is alkyl, aryl, aralkyl, heteroaryl and heteroaralkyl);

R⁴ is selected from the group consisting of hydrogen, halogen, alkyl, hydroxy, alkoxy and -NR¹³R¹⁴;

R⁵ is selected from the group consisting of hydrogen, alkyl and -C(O)R¹⁰;

R⁶ is selected from the group consisting of hydrogen, alkyl and -C(O)R¹⁰;

R⁷ is selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, -C(O)R¹⁷ and -C(O)R¹⁰; or

R⁶ and R⁷ may combine to form a group selected from the group consisting of -(CH₂)₄-, -(CH₂)₅- and -(CH₂)₆-;

with the proviso that at least one of R^5 , R^6 or R^7 must be
 $-C(O)R^{10}$;

R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl and aryl;

R^{10} is $-N(R^{11})(CH_2)_nR^{12}$ or $-NHCH_2CH(OH)CH_2R^{12}$;

R^{11} is selected from the group consisting of hydrogen and alkyl;

R^{12} is selected from the group consisting of $-NR^{13}R^{14}$, $-N^+(O)R^{13}R^{14}$, $-N(OH)R^{13}$, and $-NHC(O)R^{13}$;

R^{13} and R^{14} are independently selected from the group consisting of hydrogen, alkyl, cyanoalkyl, cycloalkyl, aryl and heteroaryl; or

R^{13} and R^{14} may combine to form a heteroalicyclic or heteroaryl group;

R^{15} is selected from the group consisting of hydrogen, hydroxy, alkoxy and aryloxy;

R^{16} is selected from the group consisting of hydroxy,
 $-C(O)R^{15}$, $-NR^{13}R^{14}$ and $-C(O)NR^{13}R^{14}$;

R^{17} is selected from the group consisting of alkyl, cycloalkyl, aryl and heteroaryl;

R^{20} is alkyl, aryl, aralkyl or heteroaryl; and

n and r are independently 1, 2, 3, or 4; or

pharmaceutically active salts of the compound of formula I; and

a pharmaceutically acceptable carrier therefor comprising 10 – 86 % w/w of one or more pharmaceutically acceptable diluents, 2 – 20 % w/w of one or more pharmaceutically acceptable binders, 2 – 20 % w/w of one or more pharmaceutically acceptable disintegrants, and 1 – 10 % w/w of one or more pharmaceutically acceptable lubricants.

2. The formulation of claim 1, wherein the salt of said indolinone is the malate salt.

3. The formulation of claim 1, wherein the salt of said indolinone is the maleate salt.

pregelatinized starch, lactose monohydrate, lactose monohydrate regular grade, mannitol, calcium phosphate and microcrystalline cellulose.

9. The formulation of claim 1, wherein each of said one or more pharmaceutically acceptable binders is selected from the group consisting of polyvinylpyrrolidone, hydroxypropylmethyl cellulose, hydroxypropylcellulose and starch.

10. The formulation of claim 1, wherein each of said one or more pharmaceutically acceptable disintegrants is selected from the group consisting of croscarmellose sodium, sodium starch glycolate, crospovidone, and starch.

11. The formulation of claim 1, wherein each of said one or more pharmaceutically acceptable lubricants is selected from the group consisting of magnesium stearate, sodium stearyl fumarate, glyceryl behenate and stearic acid.

12. The formulation of claim 1, wherein the amount of indolinone is from 5 – 55 % w/w.

13. The formulation of claim 1, wherein the amount of indolinone is from 10 – 60 % w/w.

14. The formulation of claim 1, wherein the amount of indolinone is from 15 – 50 % w/w.

15. The formulation of claim 1, wherein the amount of indolinone is from 35– 45 % w/w.

16. The formulation of claim 1, wherein the amount of indolinone is from 39 – 43 % w/w.

17. The formulation of claim 1, wherein the amount of indolinone is from 10 – 60 % w/w.

18. The formulation of claim 1, wherein the amount of indolinone is from 10 – 40 % w/w.

19. The formulation of claim 1, wherein the amount of indolinone is from 20 – 50 % w/w.

20. The formulation of claim 1, wherein the amount of indolinone is from 38 – 42 % w/w.

21. The formulation of claim 1, wherein the amount of indolinone is from 38 – 41 % w/w.

22. The formulation of claim 1, wherein the amount of indolinone is from 39 – 41 % w/w.

23. The formulation of claim 1, wherein the amount of indolinone is from 10 – 45 % w/w.

24. The formulation of claim 1, wherein the amount of indolinone is from 15 – 40 % w/w.

25. The formulation of claim 1, wherein the amount of diluent is from 10 – 80 % w/w.

26. The formulation of claim 1, wherein the amount of diluent is from 20 – 86% w/w.

27. The formulation of claim 1, wherein the amount of diluent is from 30-80 % w/w

28. The formulation of claim 1, wherein the amount of diluent is from 10 – 25 % w/w.

29. The formulation of claim 1, wherein the amount of diluent is from 25 – 50 % w/w.

30. The formulation of claim 1, wherein the amount of diluent is from 34 – 60 % w/w.
31. The formulation of claim 1, wherein the amount of diluent is from 34 – 77%.
32. The formulation of claim 1, wherein the amount of diluent is from 45-65 % w/w.
33. The formulation of claim 1, wherein the amount of diluent is from 39 – 80 % w/w
34. The formulation of claim 1, wherein the amount of diluent is from 45 – 49 % w/w.
35. The formulation of claim 1, wherein the amount of diluent is from 46 – 50 % w/w.
36. The formulation of claim 1, wherein the amount of diluent is from 45 – 48 % w/w.
37. The formulation of claim 1, wherein the amount of diluent is from 46 – 48 % w/w.
38. The formulation of claim 1, wherein the amount of binder is from 2 – 10 % w/w.
39. The formulation of claim 1, wherein the amount of binder is from 5 – 20 % w/w.
40. The formulation of claim 1, wherein the amount of binder is from 5 – 10 % w/w.
41. The formulation of claim 1, wherein the amount of binder is from 3 – 6 % w/w.

42. The formulation of claim 1, wherein the amount of binder is from 3 – 8 % w/w.
43. The formulation of claim 1, wherein the amount of binder is from 4 – 6 % w/w.
44. The formulation of claim 1, wherein the amount of binder is from 5 – 10 % w/w.
45. The formulation of claim 1, wherein the amount of binder is from 4 – 8 % w/w.
46. The formulation of claim 1, wherein the amount of binder is from 5 – 9 % w/w.
47. The formulation of claim 1, wherein the amount of binder is from 4 – 7 % w/w.
48. The formulation of claim 1, wherein the amount of binder is from 5 – 7 % w/w.
49. The formulation of claim 1, wherein the amount of disintegrant is from 2 – 10 % w/w.
50. The formulation of claim 1, wherein the amount of disintegrant is from 5 – 20 w/w.
51. The formulation of claim 1, wherein the amount of disintegrant is from 5 – 10 % w/w.
52. The formulation of claim 1, wherein the amount of disintegrant is from 4 – 8 % w/w.
53. The formulation of claim 1, wherein the amount of disintegrant is from 5 – 8 % w/w.

54. The formulation of claim 1, wherein the amount of disintegrant is from 3 – 7 % w/w.

55. The formulation of claim 1, wherein the amount of disintegrant is from 3 – 6 % w/w.

56. The formulation of claim 1, wherein the amount of disintegrant is from 4 – 6 % w/w.

57. The formulation of claim 1, wherein the amount of lubricant is from 1 – 10 % w/w.

58. The formulation of claim 1, wherein the amount of lubricant is from 0.1 – 2.5 % w/w.

59. The formulation of claim 1, wherein the amount of lubricant is from 1 – 5 % w/w.

60. The formulation of claim 1, wherein the amount of lubricant is from 0.5 – 2 % w/w.

61. The formulation of claim 1, wherein the amount of lubricant is from 1 – 2 % w/w.

62. The formulation of claim 1, wherein the amount of lubricant is from 1 – 1.5 % w/w.

63. The formulation of claim 1, wherein the amount of lubricant is from 1 – 2.5 % w/w.

64. The formulation of claim 1, wherein the amount of lubricant is from 1.3 – 1.7 % w/w.

65. The formulation of claim 1, wherein the amount of lubricant is from 1.4 – 1.8 % w/w.

66. The formulation of claim 1, wherein the amount of lubricant is from 1.3 – 1.6 % w/w.

67. The formulation of claim 1, wherein the amount of lubricant is from 1.4 – 1.6 % w/w.

68. The formulation of claim 1, wherein said diluent is mannitol.

69. The formulation of claim 1, wherein said binder is polyvinylpyrrolidone.

70. The formulation of claim 1, wherein said disintegrant is crosscarmellose sodium.

71. The formulation of claim 1, wherein said lubricant is magnesium stearate.

72. The formulation of claim 1, wherein:

R^1 is selected from the group consisting of hydrogen, halo, alkyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, $-(CH_2)_nR^{16}$ and $-C(O)NR^8R^9$;

R^2 is selected from the group consisting of hydrogen, halo, alkyl, trihalomethyl, hydroxy, alkoxy, cyano, $-NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-C(O)R^{15}$, aryl, heteroaryl, and $-S(O)_2NR^{13}R^{14}$;

R^3 is selected from the group consisting of hydrogen, halogen, alkyl, trihalomethyl, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, aryl, heteroaryl, $-NR^{13}S(O)_2R^{14}$, $-S(O)_2NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-NR^{13}C(O)OR^{14}$ and $-SO_2R^{20}$ (wherein R^{20} is alkyl, aryl, aralkyl, heteroaryl and heteroaralkyl);

R^4 is selected from the group consisting of hydrogen, halogen, alkyl, hydroxy, alkoxy and $-NR^{13}R^{14}$;

R^5 is selected from the group consisting of hydrogen and alkyl;

R^6 is $-C(O)R^{10}$ wherein R^{10} is $-NR^{11}(CH_2)_nR^{12}$ wherein:

R^{11} is hydrogen or lower unsubstituted alkyl;

n is 2 or 3; and

R^{12} is selected from the group consisting of $-NR^{13}R^{14}$, $-N^+(O)R^{13}R^{14}$, and $-N(OH)R^{13}$;

R^7 is selected from the group consisting of hydrogen, alkyl, aryl and heteroaryl;

R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl and aryl;

R^{13} and R^{14} are independently selected from the group consisting of hydrogen, alkyl, lower alkyl substituted with hydroxy, alkylamino, cyanoalkyl, cycloalkyl, aryl and heteroaryl; or

R^{13} and R^{14} may combine to form a heteroalicyclic or heteroaryl group;

R^{15} is selected from the group consisting of hydrogen, hydroxy, alkoxy and aryloxy;

R^{16} is selected from the group consisting of hydroxy, $-C(O)R^{15}$, $-NR^{13}R^{14}$ and $-C(O)NR^{13}R^{14}$; and

r is 1, 2, 3, or 4.

73. The formulation of claim 1, wherein R^6 is $-C(O)R^{10}$ wherein R^{10} is $-NHCH_2CH(OH)CH_2R_{12}$, wherein R_{12} is selected from the group consisting of $-NR^{13}R^{14}$, $-N^+(O)R^{13}R^{14}$ and $-N(OH)R^{13}$; and R^{13} and R^{14} are independently selected from the group consisting of hydrogen, alkyl, lower alkyl substituted with hydroxy, alkylamino, cyanoalkyl, cycloalkyl, aryl and heteroaryl; or R^{13} and R^{14} may combine to form a heteroalicyclic or heteroaryl group.

74. The formulation of claim 1, wherein R^6 is $-C(O)R^{10}$ wherein R^{10} is $-NR^{11}(CH_2)_nR^{12}$ wherein:

R^{11} is hydrogen or lower unsubstituted alkyl;

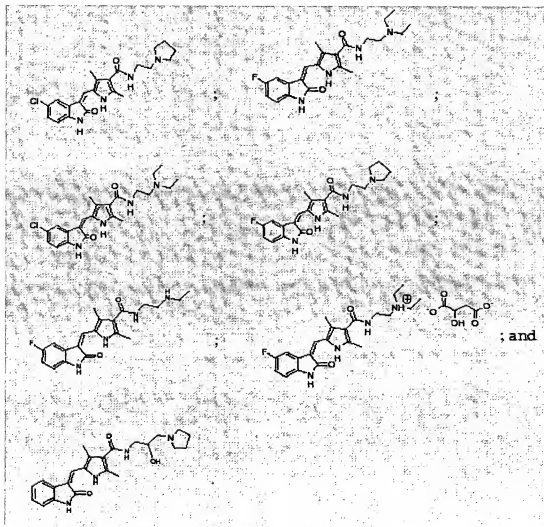
n is 2 or 3; and

R^{12} is $-NR^{13}R^{14}$ wherein R^{13} and R^{14} are independently unsubstituted lower alkyl; and

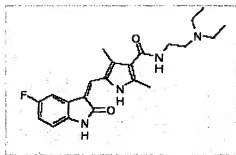
R^7 is selected from the group consisting of hydrogen, alkyl, aryl and heteroaryl.

75. The formulation of claim 1, wherein R^6 is N-(2-dimethylaminoethyl)aminocarbonyl, N-(2-diethylaminoethyl)-N-methylaminocarbonyl, N-(3-dimethylaminopropyl)aminocarbonyl, N-(2-diethylaminoethyl)aminocarbonyl, N-(2-ethylaminoethyl)aminocarbonyl, N-(3-ethylaminopropyl)aminocarbonyl, N-(2-hydroxy-3-pyrrolidin-1-yl-propyl)-aminocarbonyl, N-(2-pyrrolidin-1-yl-ethyl)-aminocarbonyl or N-(3-diethylaminopropyl)aminocarbonyl.

76. The formulation of claim 1, wherein the compound of formula is selected from the group consisting of:



77. The formulation of claim 1, wherein the compound of formula I is:



78. The formulation of claim 1, wherein said formulation comprises 15 – 60 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 25 – 75 % w/w mannitol, 4 – 8 % w/w croscarmellose sodium, 4 – 6 % w/w povidone and 0.5 – 2 % w/w magnesium stearate.

79. The formulation of claim 1, wherein said formulation comprises 30 – 50 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 35 – 60 % w/w mannitol, 5 – 8 % w/w croscarmellose sodium, 4 – 6 % w/w povidone and 1 – 2 % w/w magnesium stearate.

80. The formulation of claim 1, wherein said formulation comprises 40 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 47.5 % w/w mannitol, 6 % w/w croscarmellose sodium, 5 % w/w povidone and 1.5 % w/w magnesium stearate.

81. The formulation of claim 1, wherein said formulation comprises 10 – 16 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 65 – 80 % w/w mannitol, 5 – 10 % w/w croscarmellose sodium, 4 – 8 % w/w povidone and 1 – 2 % w/w magnesium stearate.

82. The formulation of claim 1, wherein said formulation comprises 15.2 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 72.7 % w/w mannitol, 6 % w/w croscarmellose sodium, 5.1 % w/w povidone and 1 % w/w magnesium stearate.

83. The formulation of claim 1, wherein said formulation comprises 38 – 42 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt

thereof, 45 – 49 % w/w mannitol, 4 – 8 % w/w croscarmellose sodium, 3 – 7 % w/w povidone and 1.3 – 1.7 % w/w magnesium stearate.

84. The formulation of claim 1, wherein said formulation comprises 39 – 43 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 46 – 50 % w/w mannitol, 5 – 9 % w/w croscarmellose sodium, 4 – 8 % w/w povidone and 1.4 – 1.8 % w/w magnesium stearate.

85. The formulation of claim 1, wherein said formulation comprises 38 – 41 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 45 – 48 % w/w mannitol, 4 – 7 % w/w croscarmellose sodium, 3 – 6 % w/w povidone and 1.3 – 1.6 % w/w magnesium stearate.

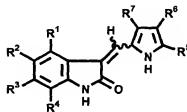
86. The formulation of claim 1, wherein said formulation comprises 39 – 43 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 46 – 50 % w/w mannitol, 5 – 9 % w/w croscarmellose sodium, 4 – 8 % w/w povidone and 1.4 – 1.8 % w/w magnesium stearate.

87. The formulation of claim 1, wherein said formulation comprises 39 – 41 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 46 – 48 % w/w mannitol, 5 – 7 % w/w croscarmellose sodium, 4 – 6 % w/w povidone and 1.4 – 1.6 % w/w magnesium stearate.

88. The formulation of claim 1, wherein said formulation comprises 39 – 43 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 46 – 50 % w/w mannitol, 5 – 9 % w/w croscarmellose sodium, 4 – 8 % w/w povidone and 0.8 – 1.5 % w/w magnesium stearate.

89. The formulation of claim 1, wherein said formulation comprises 39 – 43 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 46 – 50 % w/w mannitol, 5 – 9 % w/w croscarmellose sodium, 4 – 8 % w/w povidone and 0.8 – 1.2 % w/w magnesium stearate.

90. A solid formulation, said formulation comprising 5 – 60 % w/w of an indolinone of formula I:



(I)

wherein:

R¹ is selected from the group consisting of hydrogen, halo, alkyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, $-(CH_2)_nR^{16}$ and $-C(O)NR^8R^9$;

R² is selected from the group consisting of hydrogen, halo, alkyl, trihalomethyl, hydroxy, alkoxy, cyano, $-NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-C(O)R^{15}$, aryl, heteroaryl, and $-S(O)_2NR^{13}R^{14}$;

R³ is selected from the group consisting of hydrogen, halogen, alkyl, trihalomethyl, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, aryl, heteroaryl, $-NR^{13}S(O)_2R^{14}$, $-S(O)_2NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-NR^{13}C(O)OR^{14}$ and $-SO_2R^{20}$ (wherein R²⁰ is alkyl, aryl, aralkyl, heteroaryl and heteroaralkyl);

R⁴ is selected from the group consisting of hydrogen, halogen, alkyl, hydroxy, alkoxy and $-NR^{13}R^{14}$;

R⁵ is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R⁶ is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R⁷ is selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, $-C(O)R^{17}$ and $-C(O)R^{10}$; or

R⁶ and R⁷ may combine to form a group selected from the group consisting of $-(CH_2)_4-$, $-(CH_2)_5-$ and $-(CH_2)_6-$;

with the proviso that at least one of R⁵, R⁶ or R⁷ must be $-C(O)R^{10}$;

R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl and aryl;

R^{10} is $-N(R^{11})(CH_2)_nR^{12}$ or $-NHCH_2CH(OH)CH_2R^{12}$;

R^{11} is selected from the group consisting of hydrogen and alkyl;

R^{12} is selected from the group consisting of $-NR^{13}R^{14}$, $-N^+(O)R^{13}R^{14}$, $-N(OH)R^{13}$, and $-NHC(O)R^{13}$;

R^{13} and R^{14} are independently selected from the group consisting of hydrogen, alkyl, cyanoalkyl, cycloalkyl, aryl and heteroaryl; or

R^{13} and R^{14} may combine to form a heteroalicyclic or heteroaryl group;

R^{15} is selected from the group consisting of hydrogen, hydroxy, alkoxy and aryloxy;

R^{16} is selected from the group consisting of hydroxy, $-C(O)R^{15}$, $-NR^{13}R^{14}$ and $-C(O)NR^{13}R^{14}$;

R^{17} is selected from the group consisting of alkyl, cycloalkyl, aryl and heteroaryl;

R^{20} is alkyl, aryl, aralkyl or heteroaryl; and

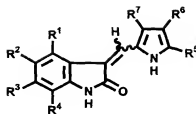
n and r are independently 1, 2, 3, or 4; or

pharmaceutically active salts of the compound of formula I; and

a pharmaceutically acceptable carrier therefor comprising 10 – 86 % w/w of one or more pharmaceutically acceptable diluents, 2 – 20 % w/w of one or more pharmaceutically acceptable binders, 2 – 20 % w/w of one or more pharmaceutically acceptable disintegrants, and 1 – 10 % w/w of one or more pharmaceutically acceptable lubricants;

with the proviso that said formulation does not comprise a surfactant and/or a flow enhancer.

91. A solid formulation, said formulation consisting essentially of 5 – 60 % w/w of an indolinone of formula I:



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, halo, alkyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, $-(CH_2)_nR^{16}$ and $-C(O)NR^8R^9$;

R^2 is selected from the group consisting of hydrogen, halo, alkyl, trihalomethyl, hydroxy, alkoxy, cyano, $-NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-C(O)R^{15}$, aryl, heteroaryl, and $-S(O)_2NR^{13}R^{14}$;

R^3 is selected from the group consisting of hydrogen, halogen, alkyl, trihalomethyl, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, aryl, heteroaryl, $-NR^{13}S(O)_2R^{14}$, $-S(O)_2NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-NR^{13}C(O)OR^{14}$ and $-SO_2R^{20}$ (wherein R^{20} is alkyl, aryl, aralkyl, heteroaryl and heteroaralkyl);

R^4 is selected from the group consisting of hydrogen, halogen, alkyl, hydroxy, alkoxy and $-NR^{13}R^{14}$;

R^5 is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R^6 is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R^7 is selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, $-C(O)R^{17}$ and $-C(O)R^{10}$; or

R^6 and R^7 may combine to form a group selected from the group consisting of $-(CH_2)_4-$, $-(CH_2)_5-$ and $-(CH_2)_6-$;

with the proviso that at least one of R^5 , R^6 or R^7 must be $-C(O)R^{10}$;

R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl and aryl;

R^{10} is $-N(R^{11})(CH_2)_nR^{12}$ or $-NHCH_2CH(OH)CH_2R_{12}$;

R^{11} is selected from the group consisting of hydrogen and alkyl;

R^{12} is selected from the group consisting of $-NR^{13}R^{14}$, $-N^+(O)R^{13}R^{14}$, $-N(OH)R^{13}$, and $-NHC(O)R^{13}$;

R^{13} and R^{14} are independently selected from the group consisting of hydrogen, alkyl, cyanoalkyl, cycloalkyl, aryl and heteroaryl; or

R^{13} and R^{14} may combine to form a heteroalicyclic or heteroaryl group;

R^{15} is selected from the group consisting of hydrogen, hydroxy, alkoxy and aryloxy;

R^{16} is selected from the group consisting of hydroxy, $-C(O)R^{15}$, $-NR^{13}R^{14}$ and $-C(O)NR^{13}R^{14}$;

R^{17} is selected from the group consisting of alkyl, cycloalkyl, aryl and heteroaryl;

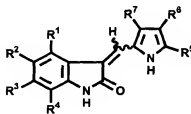
R^{20} is alkyl, aryl, aralkyl or heteroaryl; and

n and r are independently 1, 2, 3, or 4; or

pharmaceutically active salts of the compound of formula I; and

a pharmaceutically acceptable carrier therefor comprising 10 – 86 % w/w of one or more pharmaceutically acceptable diluents, 2 – 20 % w/w of one or more pharmaceutically acceptable binders, 2 – 20 % w/w of one or more pharmaceutically acceptable disintegrants, and 1 – 10 % w/w of one or more pharmaceutically acceptable lubricants.

92. A solid formulation, said formulation comprising 5 – 60 % w/w of the malate salt of an indolinone of formula I:



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, halo, alkyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, $-(CH_2)_nR^{16}$ and $-C(O)NR^8R^9$;

R^2 is selected from the group consisting of hydrogen, halo, alkyl, trihalomethyl, hydroxy, alkoxy, cyano, $-NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-C(O)R^{15}$, aryl, heteroaryl, and $-S(O)_2NR^{13}R^{14}$;

R^3 is selected from the group consisting of hydrogen, halogen, alkyl, trihalomethyl, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, aryl, heteroaryl, $-NR^{13}S(O)_2R^{14}$, $-S(O)_2NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-NR^{13}C(O)OR^{14}$ and $-SO_2R^{20}$ (wherein R^{20} is alkyl, aryl, aralkyl, heteroaryl and heteroaralkyl);

R^4 is selected from the group consisting of hydrogen, halogen, alkyl, hydroxy, alkoxy and $-NR^{13}R^{14}$;

R^5 is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R^6 is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R^7 is selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, $-C(O)R^{17}$ and $-C(O)R^{10}$; or

R^6 and R^7 may combine to form a group selected from the group consisting of $-(CH_2)_4-$, $-(CH_2)_5-$ and $-(CH_2)_6-$; with the proviso that at least one of R^5 , R^6 or R^7 must be $-C(O)R^{10}$;

R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl and aryl;

R^{10} is $-N(R^{11})(CH_2)_nR^{12}$ or $-NHCH_2CH(OH)CH_2R^{12}$;

R^{11} is selected from the group consisting of hydrogen and alkyl;

R^{12} is selected from the group consisting of $-NR^{13}R^{14}$, $-N^+(O^-)R^{13}R^{14}$, $-N(OH)R^{13}$, and $-NHC(O)R^{13}$;

R^{13} and R^{14} are independently selected from the group consisting of hydrogen, alkyl, cyanoalkyl, cycloalkyl, aryl and heteroaryl; or

R^{13} and R^{14} may combine to form a heteroalicyclic or heteroaryl group;

R^{15} is selected from the group consisting of hydrogen, hydroxy, alkoxy and aryloxy;

R^{16} is selected from the group consisting of hydroxy, $-C(O)R^{15}$, $-NR^{13}R^{14}$ and $-C(O)NR^{13}R^{14}$;

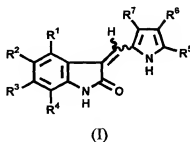
R^{17} is selected from the group consisting of alkyl, cycloalkyl, aryl and heteroaryl;

R^{20} is alkyl, aryl, aralkyl or heteroaryl; and

n and r are independently 1, 2, 3, or 4; and

a pharmaceutically acceptable carrier therefor comprising 10 – 86 % w/w of one or more pharmaceutically acceptable diluents, 2 – 20 % w/w of one or more pharmaceutically acceptable binders, 2 – 20 % w/w of one or more pharmaceutically acceptable disintegrants, and 1 – 10 % w/w of one or more pharmaceutically acceptable lubricants.

93. A solid formulation comprising an indolinone compound of formula I:



wherein:

R^1 is selected from the group consisting of hydrogen, halo, alkyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, $-(CH_2)_rR^{16}$ and $-C(O)NR^6R^9$;

R^2 is selected from the group consisting of hydrogen, halo, alkyl, trihalomethyl, hydroxy, alkoxy, cyano, $-NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-C(O)R^{15}$, aryl, heteroaryl, and $-S(O)_2NR^{13}R^{14}$;

R^3 is selected from the group consisting of hydrogen, halogen, alkyl, trihalomethyl, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, aryl, heteroaryl, $-NR^{13}S(O)_2R^{14}$, $-S(O)_2NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-NR^{13}C(O)OR^{14}$ and $-SO_2R^{20}$ (wherein R^{20} is alkyl, aryl, aralkyl, heteroaryl and heteroaralkyl);

R^4 is selected from the group consisting of hydrogen, halogen, alkyl, hydroxy, alkoxy and $-NR^{13}R^{14}$;

R^5 is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R^6 is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R^7 is selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, $-C(O)R^{17}$ and $-C(O)R^{10}$; or

R^6 and R^7 may combine to form a group selected from the group consisting of $-(CH_2)_4-$, $-(CH_2)_5-$ and $-(CH_2)_6-$; with the proviso that at least one of R^5 , R^6 or R^7 must be $-C(O)R^{10}$;

R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl and aryl;

R^{10} is $-N(R^{11})(CH_2)_nR^{12}$ or $-NHCH_2CH(OH)CH_2R^{12}$;

R^{11} is selected from the group consisting of hydrogen and alkyl;

R^{12} is selected from the group consisting of $-NR^{13}R^{14}$, $-N^+(O^-)R^{13}R^{14}$, $-N(OH)R^{13}$, and $-NHC(O)R^{13}$;

R^{13} and R^{14} are independently selected from the group consisting of hydrogen, alkyl, cyanoalkyl, cycloalkyl, aryl and heteroaryl; or

R^{13} and R^{14} may combine to form a heteroalicyclic or heteroaryl group;

R^{15} is selected from the group consisting of hydrogen, hydroxy, alkoxy and aryloxy;

R^{16} is selected from the group consisting of hydroxy, $-C(O)R^{15}$, $-NR^{13}R^{14}$ and $-C(O)NR^{13}R^{14}$;

R^{17} is selected from the group consisting of alkyl, cycloalkyl, aryl and heteroaryl;

R^{20} is alkyl, aryl, aralkyl or heteroaryl; and

n and r are independently 1, 2, 3, or 4; or
pharmaceutically active salts of the compound of formula I;
wherein the bulk density of said formulation is at least about 0.50 kg/L.

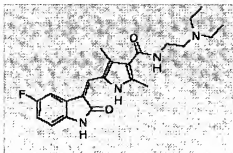
94. The formulation of 93, wherein the bulk density of said solid formulation is about 2 to about 8 fold higher than the bulk density of the indolinone compound by itself.

95. The formulation of 93, wherein the bulk density of said formulation is about 0.55, 0.56, 0.57, 0.58, 0.59, 0.60, 0.61, 0.62, 0.63, 0.64, 0.65, 0.66, 0.67, 0.69 or 0.7 kg/L.

96. The formulation of one of claims 93, wherein the ratio of tap density to bulk density of said formulation is from about 1.10 to about 1.30.

97. The formulation of claim 93, wherein the ratio is from about 1.10 to about 1.33, or about 1.10 to about 1.25, or about 1.10 to about 1.20, or about 1.10 to about 1.15.

98. The formulation of claim 93, wherein said salt of said compound is

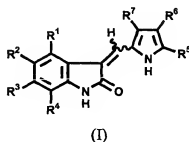


or the L-malate salt thereof.

99. The formulation of claim 93, wherein said formulation comprises 15-40% of the indolinone compound.

100. The formulation of claim 93, wherein said formulation comprises 40 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 47.5 % w/w mannitol, 6 % w/w croscarmellose sodium, 5 % w/w povidone and 1.5 % w/w magnesium stearate.

101. A solid formulation comprising an indolinone compound of formula I:



wherein:

R^1 is selected from the group consisting of hydrogen, halo, alkyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, $-(CH_2)_nR^{16}$ and $-C(O)NR^8R^9$;

R^2 is selected from the group consisting of hydrogen, halo, alkyl, trihalomethyl, hydroxy, alkoxy, cyano, $-NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-C(O)R^{15}$, aryl, heteroaryl, and $-S(O)_2NR^{13}R^{14}$;

R^3 is selected from the group consisting of hydrogen, halogen, alkyl, trihalomethyl, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, aryl, heteroaryl, $-NR^{13}S(O)_2R^{14}$, $-S(O)_2NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-NR^{13}C(O)OR^{14}$ and $-SO_2R^{20}$ (wherein R^{20} is alkyl, aryl, aralkyl, heteroaryl and heteroaralkyl);

R^4 is selected from the group consisting of hydrogen, halogen, alkyl, hydroxy, alkoxy and $-NR^{13}R^{14}$;

R^5 is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R^6 is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R^7 is selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, $-C(O)R^{17}$ and $-C(O)R^{10}$; or

R^6 and R^7 may combine to form a group selected from the group consisting of $-(CH_2)_4-$, $-(CH_2)_5-$ and $-(CH_2)_6-$;

with the proviso that at least one of R^5 , R^6 or R^7 must be

$-\text{C}(\text{O})\text{R}^{10}$;

R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl and aryl;

R^{10} is $-\text{N}(\text{R}^{11})(\text{CH}_2)_n\text{R}^{12}$ or $-\text{NHCH}_2\text{CH}(\text{OH})\text{CH}_2\text{R}^{12}$;

R^{11} is selected from the group consisting of hydrogen and alkyl;

R^{12} is selected from the group consisting of $-\text{NR}^{13}\text{R}^{14}$, $-\text{N}^+(\text{O})\text{R}^{13}\text{R}^{14}$, $-\text{N}(\text{OH})\text{R}^{13}$, and $-\text{NHC}(\text{O})\text{R}^{13}$;

R^{13} and R^{14} are independently selected from the group consisting of hydrogen, alkyl, cyanoalkyl, cycloalkyl, aryl and heteroaryl; or

R^{13} and R^{14} may combine to form a heteroalicyclic or heteroaryl group;

R^{15} is selected from the group consisting of hydrogen, hydroxy, alkoxy and aryloxy;

R^{16} is selected from the group consisting of hydroxy,

$-\text{C}(\text{O})\text{R}^{15}$, $-\text{NR}^{13}\text{R}^{14}$ and $-\text{C}(\text{O})\text{NR}^{13}\text{R}^{14}$;

R^{17} is selected from the group consisting of alkyl, cycloalkyl, aryl and heteroaryl;

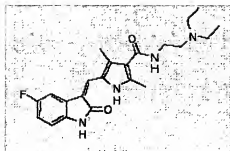
R^{20} is alkyl, aryl, aralkyl or heteroaryl; and

n and r are independently 1, 2, 3, or 4; or

pharmaceutically active salts of the compound of formula I;

wherein said formulation is in particulate form, and wherein no more than 55% of the particles have a size less than 250 microns.

102. The formulation of claim 101, wherein said salt of said compound is

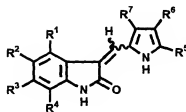


or the L-malate salt thereof.

103. The formulation of claim 101, wherein said formulation comprises 15-40% of the indolinone compound.

104. The formulation of claim 101, wherein said formulation comprises 40 % w/w of an indolinone of formula I, or a pharmaceutically acceptable salt thereof, 47.5 % w/w mannitol, 6 % w/w croscarmellose sodium, 5 % w/w povidone and 1.5 % w/w magnesium stearate.

105. A solid formulation comprising an indolinone compound of formula I:



(I)

wherein:

R¹ is selected from the group consisting of hydrogen, halo, alkyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, $-(CH_2)_nR^{16}$ and $-C(O)NR^8R^9$;

R² is selected from the group consisting of hydrogen, halo, alkyl, trihalomethyl, hydroxy, alkoxy, cyano, $-NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-C(O)R^{15}$, aryl, heteroaryl, and $-S(O)_2NR^{13}R^{14}$;

R³ is selected from the group consisting of hydrogen, halogen, alkyl, trihalomethyl, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, aryl, heteroaryl, $-NR^{13}S(O)_2R^{14}$, $-S(O)_2NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-NR^{13}C(O)OR^{14}$ and $-SO_2R^{20}$ (wherein R²⁰ is alkyl, aryl, aralkyl, heteroaryl and heteroaralkyl);

R⁴ is selected from the group consisting of hydrogen, halogen, alkyl, hydroxy, alkoxy and $-NR^{13}R^{14}$;

R⁵ is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R⁶ is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R^7 is selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, $-C(O)R^{17}$ and $-C(O)R^{10}$; or

R^6 and R^7 may combine to form a group selected from the group consisting of $-(CH_2)_4-$, $-(CH_2)_5-$ and $-(CH_2)_6-$; with the proviso that at least one of R^5 , R^6 or R^7 must be $-C(O)R^{10}$;

R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl and aryl;

R^{10} is $-N(R^{11})(CH_2)_nR^{12}$ or $-NHCH_2CH(OH)CH_2R^{12}$;

R^{11} is selected from the group consisting of hydrogen and alkyl;

R^{12} is selected from the group consisting of $-NR^{13}R^{14}$, $-N^+(O)R^{13}R^{14}$, $-N(OH)R^{13}$, and $-NHC(O)R^{13}$;

R^{13} and R^{14} are independently selected from the group consisting of hydrogen, alkyl, cyanoalkyl, cycloalkyl, aryl and heteroaryl; or

R^{13} and R^{14} may combine to form a heteroalicyclic or heteroaryl group;

R^{15} is selected from the group consisting of hydrogen, hydroxy, alkoxy and aryloxy;

R^{16} is selected from the group consisting of hydroxy, $-C(O)R^{15}$, $-NR^{13}R^{14}$ and $-C(O)NR^{13}R^{14}$;

R^{17} is selected from the group consisting of alkyl, cycloalkyl, aryl and heteroaryl;

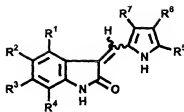
R^{20} is alkyl, aryl, aralkyl or heteroaryl; and

n and r are independently 1, 2, 3, or 4; or

pharmaceutically active salts of the compound of formula I;

wherein said formulation is in particulate form, and wherein the mean particle size is between 106 and 250 microns.

106. A solid formulation comprising the malate salt of an indolinone compound of formula I:



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, halo, alkyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, $-(CH_2)_nR^{16}$ and $-C(O)NR^8R^9$;

R^2 is selected from the group consisting of hydrogen, halo, alkyl, trihalomethyl, hydroxy, alkoxy, cyano, $-NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-C(O)R^{15}$, aryl, heteroaryl, and $-S(O)_2NR^{13}R^{14}$;

R^3 is selected from the group consisting of hydrogen, halogen, alkyl, trihalomethyl, hydroxy, alkoxy, $-(CO)R^{15}$, $-NR^{13}R^{14}$, aryl, heteroaryl, $-NR^{13}S(O)_2R^{14}$, $-S(O)_2NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-NR^{13}C(O)OR^{14}$ and $-SO_2R^{20}$ (wherein R^{20} is alkyl, aryl, aralkyl, heteroaryl and heteroaralkyl);

R^4 is selected from the group consisting of hydrogen, halogen, alkyl, hydroxy, alkoxy and $-NR^{13}R^{14}$;

R^5 is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R^6 is selected from the group consisting of hydrogen, alkyl and $-C(O)R^{10}$;

R^7 is selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, $-C(O)R^{17}$ and $-C(O)R^{10}$; or

R^6 and R^7 may combine to form a group selected from the group consisting of $-(CH_2)_4-$, $-(CH_2)_5-$ and $-(CH_2)_6-$;

with the proviso that at least one of R^5 , R^6 or R^7 must be $-C(O)R^{10}$;

R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl and aryl;

R^{10} is $-N(R^{11})(CH_2)_nR^{12}$ or $-NHCH_2CH(OH)CH_2R^{12}$;

R^{11} is selected from the group consisting of hydrogen and alkyl;

R^{12} is selected from the group consisting of $-NR^{13}R^{14}$, $-N^+(O)R^{13}R^{14}$, $-N(OH)R^{13}$, and $-NHC(O)R^{13}$;

R^{13} and R^{14} are independently selected from the group consisting of hydrogen, alkyl, cyanoalkyl, cycloalkyl, aryl and heteroaryl; or

R^{13} and R^{14} may combine to form a heteroalicyclic or heteroaryl group;

R^{15} is selected from the group consisting of hydrogen, hydroxy, alkoxy and aryloxy;

R^{16} is selected from the group consisting of hydroxy, $-C(O)R^{15}$, $-NR^{13}R^{14}$ and $-C(O)NR^{13}R^{14}$;

R^{17} is selected from the group consisting of alkyl, cycloalkyl, aryl and heteroaryl;

R^{20} is alkyl, aryl, aralkyl or heteroaryl; and

n and r are independently 1, 2, 3, or 4;

wherein the bulk density of said solid formulation is about 2 to about 8 fold higher than the bulk density of the malate salt of the indolinone compound by itself.